Table 1. Risk factors for patello-femoral cartilage loss at 6 months

| Risk factor | Reference | Adjusted Odds Ratio[3] (95% confidence intervals) |
|---|---|---|
| Effusion (WORMS ≥ 1)[1] | Effusion absence (WORMS score = 0) | 3.54 (1.30-9.64)* |
| Synovitis (modified WORMS ≥ 1)[1] | Synovitis absence (modified WORMS score = 0 in both synovitis subregions) | 0.79 (0.28-2.07) |
| Prevalent cartilage damage (WORMS ≥ 2)[2] | No cartilage damage in subregion (WORMS score = 0 or 1) | 4.32 (1.35-13.85)* |
| BML (WORMS ≥ 1)[2] | No BML in subregion (WORMS score =0) | 1.61 (0.67-3.84) |

[1]cartilage loss at 6 months in any of 10 TF subregions
[2]cartilage loss at 6 months in same subregion
[3]multi-adjusted GEE model accounting for correlations within and between knees, and adjusted for age, gender, BMI, and treatment
* statistically significant at p ≤ 0.05

Table 2. Risk factors for tibio-femoral cartilage loss at 6 months

| Risk factor | Reference | Adjusted Odds Ratio[4] (95% confidence intervals) |
|---|---|---|
| Effusion[1] (WORMS ≥ 1)[1] | Effusion absence (WORMS score = 0) | 1.79 (0.76-4.23) |
| Synovitis[1] (modified WORMS ≥ 1)[1] | Synovitis absence (modified WORMS score = 0) | 0.68 (0.32-1.45) |
| Meniscal damage[2] | No meniscal damage | 1.98 (0.76-5.15) |
| Meniscal extrusion[2] | No meniscal extrusion | 3.62 (1.29-10.12)* |
| Prevalent cartilage damage (WORMS ≥ 2)[3] | Absence of cartilage damage in subregion (WORMS =0 or 1) | 15.90 (5.08-49.79)* |
| BML (WORMS ≥ 1)[3] | No BML in subregion (WORMS =0) | 4.58 (1.08-19.44)* |
| Presence of BML and ipsi-compartmental extrusion | Absence of BML and concomitant ipsi-compartmental extrusion[2] | 0.13 (0.02-0.67)** |

[1]cartilage loss in any of 10 TF subregions
[2]cartilage loss in same compartment as meniscal damage or extrusion (5 subregions medial or lateral)
[3]cartilage loss in same subregion
[4]multi-adjusted GEE model accounting for correlations within and between knees, and adjusted for age, gender, BMI, and treatment
* statistically significant at p ≤ 0.05

at 6 months were baseline presence of effusion and prevalent cartilage damage in the same subregion (Table 1). Risk factors for TF cartilage loss were baseline ipsi-compartmental meniscal extrusion, prevalent BMLs and cartilage damage in same subregion. The interaction of the presence of both BML and ipsi-compartmental meniscal extrusion resulted in a less than expected multiplicative effect on cartilage loss (Table 2).

**Conclusions:** Cartilage loss over 6 months is rare, but may be detected semiquantitatively by MRI in a small proportion of subjects. The strongest predictors of PF cartilage loss were presence of baseline effusion and prevalent cartilage damage in the same subregion. Predictors of TF cartilage loss were prevalent cartilage damage, prevalent BMLs and meniscal extrusion. Cartilage loss was less likely to occur in compartments without meniscal extrusion and concomitant ipsi-compartmental BMLs. MRI-based structural risk factors for PF cartilage loss seem to differ from the TF joint.

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### LONGITUDINAL SENSITIVITY TO CHANGE IN CARTILAGE MORPHOLOGY OF OAI KNEES - FROM HEALTHY REFERENCE TO LATE STAGE RADIOGRAPHIC OA

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**Purpose:** Clinical trials in OA have generally excluded participants with late- or end-stage radiographic OA (ROA), because no further reduction in JSW can be expected at this stage. Participants with late- or end-stage ROA (i.e. Kellgren-Lawrence grade [KLG] 4), however, are of high interest, because they are likely to receive total knee arthroplasty in the near future, representing a well established clinical endpoint. The Objective was to study the longitudinal rate of (and sensitivity to) change in femorotibial cartilage morphology over 12 months, across various disease stages ranging from healthy reference knees to late-stage ROA knees.

**Methods:** One knee in each of 831 Osteoarthritis Initiative (OAI) participants (public use data sets 0.E.1 and 1.E.1. [imaging] and 0.2.2 [clinical]) was studied: 112 healthy without risk factors of knee OA and 719 with ROA (310 calculated KLG [cKLG] 2, 300 cKLG3, and 109 cKLG4). Segmentation of femorotibial cartilage plates and ordered values (OV: Buck et al. ACR 2009) of subregional thickness change were obtained from coronal FLASH MR images acquired at baseline and at 12 months, the operators being blinded to the time point.

**Results:** Healthy knees displayed small thickness changes (<0.7%) in femorotibial cartilage plates and subregions; OVs were symmetrically distributed around zero (Table 1). cKLG2 knees also showed small (<1%) changes, which did not significantly differ from healthy knees. cKLG3 knees, however, displayed cartilage thinning of up to 2.5% (central femur) and cKLG 4 knees of up to 3.9% (external tibia), with OVs 1-10 differing significantly from healthy knees. The OV approach was more sensitive to detecting significant differences between cKLG groups (minimal $p=5.5\times10^{-14}$; Kruskall Wallis) than a region-based approach (minimal $p=1.2\times10^{-5}$).

Table 1. Ordered values (OV) of longitudinal subregional cartilage thickness change over 12 months

| | Healthy controls (n=112) | | | cKLG 2 (n=310) | | | cKLG 3 (n=300) | | | cKLG 4 (n=109) | | | Kruskal-Wallis |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | MC | SD | MC% | MC | SD | MC% | MC | SD | MC% | MC | SD | MC% | |
| OV 1 | -121 | 81 | -6.2 | -137 | 104 | -6.6 | -180* | 144 | -9.4 | -200* | 117 | -12.5 | 5.54E-014 |
| OV 2 | -80 | 45 | -4.3 | -98 | 80 | -5.3 | -126* | 95 | -7.3 | -139* | 86 | -8.7 | 6.03E-013 |
| OV 3 | -60 | 42 | -3.3 | -69 | 50 | -3.7 | -95* | 78 | -5.4 | -108* | 71 | -7.3 | 4.01E-013 |
| OV 4 | -46 | 38 | -2.6 | -53 | 43 | -2.9 | -73* | 61 | -4.2 | -85* | 60 | -6.3 | 8.43E-011 |
| OV 5 | -31 | 36 | -1.7 | -40 | 40 | -2.1 | -57* | 55 | -3.2 | -68* | 55 | -4.8 | 1.06E-009 |
| OV 6 | -20 | 36 | -1.2 | -29 | 39 | -1.6 | -43* | 50 | -2.5 | -53* | 49 | -3.8 | 6.21E-009 |
| OV 7 | -11 | 36 | -0.6 | -19 | 37 | -1.0 | -31* | 45 | -1.8 | -40* | 47 | -2.8 | 9.12E-008 |
| OV 8 | -1 | 35 | 0.0 | -9 | 36 | -0.5 | -19* | 43 | -1.1 | -27* | 45 | -1.8 | 2.95E-006 |
| OV 9 | 8 | 34 | 0.4 | 1 | 34 | 0.0 | -7* | 42 | -0.4 | -16* | 44 | -1.2 | 7.88E-006 |
| ..... > | | | | | | | | | | | | | |
| OV 16 | 124 | 83 | 6.1 | 112 | 55 | 5.8 | 116 | 71 | 6.5 | 118 | 79 | 7.7 | 0.453 |

MC = mean change in μm, SD = standard deviation of the change, MC% = mean change in %.
*Significant difference from healthy controls (Mann-Whitney U test at p<0.0167 (global p<0.05 for 3 tests)).

**Conclusions:** MR imaging-based cartilage thickness measurement displays high rates of loss at late stage ROA (knees with JSN) and small rates, indistinguishable from healthy controls, in early ROA (knees without JSN). From the perspective of sensitivity to change, cKLG4 subjects need not to be excluded from clinical trials that use MRI-based quantitative cartilage morphology as an endpoint, in particular when an OV approach is employed. This provides opportunity to study progression (cartilage thinning) closely prior to knee arthroplasty.

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### TIBIO-FEMORAL CONTACT AREA QUANTIFICATION FOR INVESTIGATING EARLY OSTEOARTHRITIS AND PROGNOSIS OF CARTILAGE LOSS

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**Purpose:** To minimize the peak stress in a synovial joint, a uniform load distribution over a large contact area seems desirable. The 'contact area' in the tibio-femoral joint we defined as the cartilage-cartilage contact area but not cartilage-meniscus contact area. We investigated the cross-sectional relationship between the medial tibio-femoral contact area (CA) and the degree of radiographic osteoarthritis (ROA) and the CA's ability to predict cartilage loss.

**Methods:** The study cohort contained 159 subjects with age range 21-81 (mean 56) and BMI 19-38 (mean 26). The Magnetic Resonance Imaging (MRI) scans of both knees for each subject were acquired using an Easote C-span scanner of field strength 0.18T. Radiographs were acquired using the SynaFlex from Synarc for grading the degree of ROA by the Kellgren